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Metrological traceability in clinical laboratory

Rastreabilidade metrológica no laboratório clínico

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ABSTRACT

Introduction: Metrological traceability is a little-known and little-discussed metrology theme in clinical laboratories, although it is the basis for comparable results. It is associated with certified reference material (CRM) and reference method (RMet). When it is used in the supply chain by diagnostic kit manufacturers, it ensures accuracy of the results yielded by laboratories. **Objective:** This study shows the availability of information on metrological traceability provided by diagnostic kit manufacturers. **Method:** It was done with the information obtained in kits of glucose, urea, creatinine, uric acid and cholesterol participants in a proficiency testing program throughout 2012 and 2013. **Results and conclusion:** In the research, 18 producers of reference materials (RMs) and 204 measurands available for laboratory medicine were found. In the study of metrological traceability, the preferential use of CRM was demonstrated by kit manufacturers (glucose 60%, urea 69%, creatinine 60%, uric acid 50%, and cholesterol 43%). An important factor is that there are a significant number of kits that do not report traceability (glucose 16%, urea 19%, creatinine 16%, uric acid 13%, and cholesterol 5%), although it is a requirement for product registration in Brazil. We hope that this study will contribute to sensitize the laboratory community to the need for a more comprehensive knowledge of this subject, and that it will stimulate institutions involved in the dissemination of knowledge in laboratory medicine to hold discussions on this topic.

Key words: laboratory chemicals; indicators and reagents.

INTRODUCTION

Metrology is the area of knowledge that deals with measurement; it is also known as science of measurement[1, 2]. The word comes from the Greek métron, which means measure or evaluate; and logos, reason, study[3]. Metrological traceability is a topic in metrology that links a measurement result with a chain of comparisons at the highest level of metrological reliability, promoting comparability of results[1, 4].

Issues related to metrological traceability, such as reference material (RM), certified reference material (CRM) and reference method (RMet) are little known or discussed in Brazilian clinical laboratories. However, the use of these concepts is associated with the results of measurements made by the laboratory, and is the basis for comparable results between laboratories[4-6].

In clinical laboratories, the term traceability is usually related to quality. In this regard, it is associated with the origin of diagnostic kits, inputs, sample custody chain, or identification of professionals involved in the different steps of the analytical process. As already mentioned, another concept of traceability, metrological traceability, is not related to quality, but to measurement[7].

In the context of laboratory medicine, metrological traceability links measurement results of a patient's sample with a reference, and, thus, makes these measurements comparable among different systems (or assays), places, and times in which they were conducted[4, 8]. Metrological traceability is a requirement in all international standards intended for use in clinical laboratories, such as the International Organization for Standardization (ISO) 15189[9], ISO 22870[10] and ISO 17025[11]. We can ensure metrological traceability of a test result obtained by a diagnostic kit is by means of CRM or RMet when input and/or diagnostic kits are produced.

These terms have specific definitions. RMet is defined in the International Vocabulary of Metrology (VIM)[1] as a measurement procedure considered capable of providing

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measurement results adequate for veracity assessment[2]. The ISO Guide 30[12] defines RM as "material, sufficiently homogeneous and stable with respect to one or morespecified properties, which has been established to be fit for its intended use in a measurement process"; and, CRM as "RM characterized by a metrologically valid procedure for one or more specified properties, accompanied by an RM certificate that provides the value of the specified property, its associated uncertainty, and a statement of metrological traceability".

RM is a more general term that comprises materials for use in quality control (QCM) and also the CRMs. RMs have several uses and applications (**Table 1**), according to its characteristics and purpose of use, as calibration of a measurement system, evaluation of a measurement process, validation, verification, method development, quality assurance, among others[2, 12-15]. CRM is a term included in the RM category, with a more specific use. CRMs are more elaborate materials, characterized by their chemical structures or microbiological species, and by their property values defined by a metrologically valid procedure[15].

TABLE 1 – Use associated with RMs

RM	
QCM	CRM
Quality control	Value assignment
Accuracy assessment	Calibration
Quality assurance	Precision assessment
	Validation/development of methods
	Metrological traceability

Source: ISO Guide 33:2015[2]; Emons H (2006)[16].

RMs: reference materials; QCM: quality control material; CRM: certified reference material.

It is important to note that the terms standard, measuring standard, analytical standard, calibration standard, and calibrator used in the clinical laboratory are synonymous with RM[15, 16].

The increasing demand for reliability and accuracy in the results obtained by analytical and metrological techniques have increased the demand for CRM for use in the validation of measurement methods and calibrations[17].

There are currently two international databases that offer information on RM producers and RMets: the Code d'Indexation des Matériaux de Référence (COMAR)[18] and the Bureau International des Poids et Mesures (BIPM)[19]. COMAR is a free-of-charge database aimed at disseminating information about RMs available in the world. It maintains cooperation with ISO/REMCO Committee on reference materials, and international metrology institutes. BIPM[19] is an institution aimed at supplying the basis for a worldwide unique and coherent system of measures, which are traceable to the International System of Units (SI). It works through the International Committee of Weights and Measures (CIPM), which cooperates with other international organizations responsible for metrology, accreditation, and normalization, such as ISO, International Laboratory Accreditation Cooperation (ILAC) and International Organization of Legal Metrology (OIML). In 2012 BIPM created the Joint Committee for Traceability in Laboratory Medicine (JCTLM), which is responsible for the area of clinical laboratories. In its webpage this committee lists CRM producers and their respective measurands, besides reference methods[20, 21].

In 2000, the metrology institute of the United States, the National Institute of Standards & Technology (NIST), RM producer, published a study over the economic impact of CRM use in cholesterol assays[22]. This study demonstrates the importance and the necessity of CRM use by manufacturers of diagnostic kits to ensure accuracy and quality of the results yielded by clinical laboratories. Additionally, the use of CRM decreases production costs of measurement systems, besides ensuring metrological traceability in the supply chain.

OBJECTIVE

Considering this scenario, this work aims at listing the institutions that produce RM for clinical laboratories, and verify the existence of information on metrological traceability of diagnostic kits commercialized in Brazil for the measurands glucose, urea, creatinine, uric acid, and cholesterol.

METHOD

Sources of information about MRC producers and RMet

For information about MR producers, the international data bases COMAR (www.comar.bam.de) and BIPM (www.bipm.org) were consulted. For information about RMets, JCTLM (www.bipm.org/jctlm) was consulted.

Sources of information about products (CRM)

Consultations on CRM products available for clinical laboratories were hold on the websites of JCTLM (www.bipm.org/jctlm), COMAR (www. comar.bam.de) and American Type Culture Collection (ATCC) (www.atcc.org).

Information on metrological traceability of diagnostic kits

Instructions for use of diagnostic kits or calibrators were used to obtain information about metrological traceability. These documents are available on the manufacturers' websites or were provided by the scientific advisory body of the diagnostic companies.

Selection of measurands

The option for the measurands glucose, urea, creatinine, uric acid and cholesterol as object of the study was taken because these are biochemical tests ordered in large numbers in clinical laboratories. A second criterion was the ascertainment of the variety of different diagnostic kits commercialized in the diagnostic market for these measurands.

Selection of diagnostic kits

We selected the analytical systems and/or diagnostic kits reported by laboratories participating in a proficiency testing program of ControlLab, to whom we thank for the courtesy of providing these pieces of information. This study was carried out during 2012 and 2013, when results of eight cycles of the program were compiled.

For analysis purposes, the analytical systems and/or diagnostic kits were classified according to categories of metrological traceability, as follows:

- CRM category – diagnostic kits that use CRM in their manufacturing;
- RMet category – diagnostic kits that use RMet in their manufacturing;
- CRM + RMet category – diagnostic kits that use CRM and RMet in their manufacturing;
- N-Info category – diagnostic kits that did not have metrological traceability or about which it was not possible to obtain information.

Finally, in order to make the article clearer, we presented the definition of some terms used in this text:

- measurand – means "what is intended to be measured"[1]. Synonymous with "analyte";
- diagnostic kit[23] – group of reagents (kit) that permits the detection or the quantification of a certain measurand;
- analytical system[9] – group that comprises equipment and a diagnostic kit.

RESULTS

Table 2 lists the institutions producers of RMs; **Table 3**, the analytes (measurands) produced by these institutions.

Table 4 displays the RMets, besides the principles of the methods listed by JCTLM for the studied measurands. **Table 5** shows the methods chosen by producers for the investigated analytical systems.

TABLE 2 – RM producers

Name (Acronym)	Country
Centro Nacional de Metrologia (CENAM)	Mexico
National Institute of Metrology, Quality and Technology (Inmetro)	Brazil
Institute for Reference Materials and Measurements (IRMM)	European Union
LGC Limited (LGC)	United Kingdom
National Institute for Biological Standards and Control (NIBSC)	United Kingdom
National Institute of Metrology (NIM)	China
National Institute of Standards and Technology (NIST)	USA
National Measurement Institute, Australia (NMIA)	Australia
National Metrology Institute of Japan (NMIJ)	Japan
Reference Material Institute for Clinical Chemistry Standards (ReCCS)	Japan
Health Sciences Authority (HSA)	Singapore
National Institute for Environmental Studies, Center for Environmental (NIES)	Japan
Korea Research Institute of Standards and Science (KRISS)	South Korea
Radiometer Analytical S.A.S. (Ra)	France
Centre National de Référence des Légionelles (CNRL)	France
IAEA Analytical Quality Control Services (IAEA)	Austria
National Institute of Public Health (NIPH)	Czech Republic
American Type Culture Collection (ATCC)	USA

Sources: JCTLM, COMAR, and ATCC.

RM: reference material.

TABLE 3 – List of measurands for which there are RM/CRM

Anti-C antibody	Chlorine	IgM	Serine
Anti-D antibody	Cobalt	Iodine	Sodium
Arsenious acid	Copper	Isoleucine	T3
Ascorbic acid	Cocaine	LDH	T4
Aspartic acid	Codeine	L-alanine	Tacrolimus
Dimethylarsinic acid	Cholesterol	L-arginine	Thallium
Folic acid	HDL-cholesterol	Legionella DNA	Theophylline
Glutamic acid	LDL-cholesterol	Leucine	Testosterone
Hippuric acid	Cholinesterase	L-phenylalanine	THC-9-COOH
L-aspartic acid	Cortisol	B lymphocyte	Thyroglobulin
L-glutamic acid	Creatinine	T lymphocyte	Thorium
Monomethylarsonic acid	Chromium	Lipase	Transferrin
Uric acid	DHEA	Lysine	TRF
Valproic acid	Diclofenac sodium	L-isoleucine	Transthyretin (TTR)
ADA1	Digoxin	Lithium	Threonine
Alanine	DNA test for BCR-ABL	L-leucine	Triglycerides
Albumin	DNA quantification	L-lysine	Trimethylarsine (oxide)
Albumin (bovine serum)	Trace elements (Pb, ...)	L-proline	Triolein
Alpha-1-acid glycoprotein	Estradiol (17-beta)	L-valine	Tripalmitin
AFP	Estradiol (18-beta)	Macroglobulin (A2M)	Thromboplastin
Alpha-tocopherol	Ethanol	Magnesium	Troponin I
ALT	Ethosuximide	Manganese	Uranium
Amylase	Factor II (prothrombin)	MDA	Urea
Androstenedione	Factor IX	MDMA	Valine
Amphetamine	Factor V	Mercury	Vanadium
Antimony	Factor VII	Methamphetamine	Vitamin D2 (25)
Alpha-1 antitrypsin (AAT)	Factor VIII	Methionine	Vitamin D3 (25)
Antithrombin	Factor X	Metronidazole	Vanillylmandelic acid (VMA)
Apolipoprotein A1	Factor XI	Molybdenum	Von Willebrand factor
Arginine	Factor XIII	Morphine	Zeaxanthin
Arsenic	Phencyclidine	Nickel	Zync
Arsenocholine	Phenylalanine	Nitrate	*A. laidlawii*
AST	Phenytoin	19-Norandrosterone	*A. brasiliensis*
Barium	Phenobarbital	PAP	*B. subtilis*
Benzoylmethylecgonine	Fibrinogen	PCR	*C. albicans*
Beryllium	Alkaline phosphatase	C-peptide	*C. sporogenes*
Beta-cryptoxanthin	Gamma-tocopherol	Perchlorate	*E. coli*
Bilirubin	GGT	pH	*K. rhizophila*
C3	Glycerides	Platinum	*M. arginini*
C4	Glycine	Potassium	*M. hominis*
Cadmium	Glucose	Primedone	*M. hyorhinis*
Calcium	Haptoglobin	Progesterone	*M. orale*
Captopril	HbA1c	Proline	*M. pneumoniae*
Carbamazepine	Glycated hemoglobin	Protein C	*M. synoviae*
Cesium	Heroin	Protein S	*M. fermentans*
Lead	Histidine	Prothrombin (fragment)	*M. salivarium*
Cyanhemoglobin	HIV molecular marker	Prothrombin	*P. aeroginosa*
Cystatin C	HLA allo-antibody	PSA	*S. epidermidis*
Cystatin	Homocysteine	Pseudoephedrine	*S. cerevisiae*
CK	IgA	Retinol	*S. enterica*
Chloramphenicol	IgG	Selenium	*S. aureus*

Sources: JCTLM, COMAR, and ATCC.

ADA: adenosine deaminase; AFP: alpha-fetoprotein; ALT: alanine transaminase ; AST: aspartate transaminase; C3: complement component 3; C4: complement component 4; CK: creatine kinase; DHEA: dehydroepiandrosterone; DNA: deoxyribonucleic acid; GGT: gamma-glutamyl transferase ; HbA1c: glycated hemoglobin; HIV: human immunodeficiency virus; HLA: human leukocyte antigen; IgA: immunoglobulin A; IgG: immunoglobulin G ; IgM: immunoglobulin M; LDH: lactate dehydrogenase; MDA: methylenedioxyamphetamine; MDMA: 3,4-methylenedioxymethamphetamine; PAP: prostatic acid phosphatase; PCR: C-reactive protein; PSA: prostate-specific antigen; T3: triiodothyronine; T4: thyroxine; THC-9-COOH: tetrahydrocannabinol carboxylic acid; TFR: transferrin receptor.

TABLE 4 – List of RMets for the measurands glucose, urea, creatinine, uric acid, and cholesterol

Measurand	Reference method/procedure	Method principle
Glucose	Japan Society of Clinical Chemistry	Enzymatic
	German Society of Clinical Chemistry	ID/GC/MS
	National Institute of Standards & Technology	ID/GC/MS
	University of Ghent	ID/GC/MS
	Center for Disease Control and Prevention	Spectrophotometry
Urea	German Society of Clinical Chemistry	ID/GC/MS
	National Institute of Standards & Technology	ID/GC/MS
	Center for Disease Control and Prevention	Spectrophotometry
Creatinine	German Society of Clinical Chemistry	ID/GC/MS
	National Institute of Standards & Technology	ID/GC/MS, ID-LC/MS
	University of Ghent	ID/GC/MS
	National Institute of Metrology (China)	ID/LC/MS, ID/LC/MS/MS
	Org-022	ID-LC/MS
	Isotope dilution LCMS surface enhanced Raman scattering (ID/SERS)	ID/SERS
Uric acid	German Society of Clinical Chemistry	ID/GC/MS
	National Institute of Standards & Technology	ID/GC/MS
	University of Ghent	ID/GC/MS
	National Institute of Metrology (China)	ID/LC/MS, ID/LC/MS/MS
Cholesterol	NCCL	HPLC, ID-LC/MS/MS
	Centers for Disease Control and Prevention	ID/GC/MS
	German Society of Clinical Chemistry	ID/GC/MS
	National Institute of Standards & Technology	ID/GC/MS
	University of Ghent	ID/GC/MS
	Org-005	Isotope dilution LCMS
	CDC Abell-Kendall method	Spectrophotometry

Source: List of BIPM/JCTLM[20].

RMets: reference methods.

TABLE 5 – RMets used in the analytical systems of the investigated glucose, urea, creatinine, and cholesterol

System (supplier)	Glucose	Urea	Creatinine	Uric acid	Cholesterol
Advia (Siemens)	NCCLS	NCCLS; enzymatic	AACC, HPLC	CDC, uricase	NCCLS; Abell-Kendall modified
Architect/Aeroset (Abbott)	---[a]	---[a]	---[a]	---[a]	Abell-Kendall
Beckman	---[a]	---[a]	---[a]	-	ID-MS and CDC
Cobas (Roche)	ID-MS	ID-MS	ID-MS	ID-MS	ID-MS or Abell-Kendall
Dialab	ID-MS	---[a]	CG-IDMS	GC ID-MS	GC ID-MS
Dimension (Dade Behring)	---[a]	---[a]	---[a]	---[a]	Abell-Kendall of CDC
Ebram	---[a]	CLSI	CLSI	CLSI	CLSI
Hitachi Cobas (Roche)	ID-MS	---[a]	ID-MS	ID-MS	ID-MS or Abell-Kendall
Integra (Roche)	ID-MS	---[a]	---[a]	ID-MS	ID-MS and Abell-Kendall
Kovalent	ID-MS	---[a]	GC-IDMS	GC ID-MS	GC ID-MS
Olympus	---[a]	---[a]	---[a]	ID-MS	Abell-Kendall

Source: Information from package inserts/instructions, or provided by the diagnostic enterprises.

RMets: reference methods; [a]: use of CRM; CRM: certified reference material.

Table 6 presents the informed metrological traceability reported by the laboratories participating in the proficiency testing program of ControlLab, in 2012 and 2013, for the studied measurands. The **Figure** is a summary of Table 6, presenting the percentages of analytical systems that use CRM, RMet, CRM + RMet, and N-Info.

DISCUSSION

In the survey of RM producers and products made available for the area of clinical laboratory, 18 institutions (Table 2) and 204 analytes (Table 3) produced by these institutions were found,

TABLE 6 – Metrological traceability of analytical systems reported by laboratories participating in the proficiency testing program

Analytical system (supplier)	Glucose	Urea	Creatinine	Uric acid	Cholesterol
ABX (Horiba)	CRM	CRM	CRM	CRM	---[b]
Advia (Siemens)	RMet	RMet	RMet	RMet	RMet
Architect/Aeroset (Abbott)	CRM	CRM	CRM	CRM	RMet
Beckman	CRM	CRM	CRM	RMet	CRM + RMet
BioclinQuibasa (Bioclin)	CRM	CRM	CRM	CRM	CRM
Biosystems	CRM	CRM	CRM	CRM	CRM
Biotécnica	CRM	CRM	CRM	CRM	CRM
Cobas (Roche)	RMet	RMet	RMet	RMet	RMet
Dialab	RMet	CRM	CRM + RMet	RMet	RMet
Dimension (Dade Behring)	CRM	CRM	CRM	CRM	CRM + RMet
Doles	N-Info[a]	N-Info[a]	N-Info[a]	N-Info[a]	---[b]
Ebram	CRM	RMet	RMet	RMet	RMet
Elitech SL (Elitech)	CRM	CRM	CRM	CRM	CRM
Gold Analisa (Gold)	CRM	CRM	CRM	CRM	CRM
Hitachi Cobas (Roche)	RMet	CRM	RMet	RMet	RMet
In Vitro Human (In Vitro)	CRM	CRM	CRM	CRM	CRM
Integra (Roche)	RMet	CRM	CRM	RMet	RMet
Katal	N-Inf[a]	N-Inf[a]	N-Inf[a]	N-Inf[a]	N-Inf[a]
Kovalent	RMet	CRM	RMet	RMet	RMet
Laborclin	N-Info[a]	N-Info[a]	N-Info[a]	N-Info[a]	---[b]
Laborlab	N-Info[a]	N-Info[a]	N-Info[a]	---[b]	---[b]
Labtest	CRM	CRM	CRM	CRM	CRM
Olympus	CRM	CRM	CRM	RMet	CRM
Vida Biotecnologia	---[b]	N-Info[a]	---[b]	---[b]	---[b]
Vitros (Ortho)	CRM	CRM	CRM	CRM	CRM
Wiener	CRM	CRM	CRM	CRM	CRM

Source: package inserts of diagnostic kits.

CRM: certified reference method; RMets: reference methods; N-Info[a]: no information about the use of CRM or RMet; [b]: the diagnostic kit does not appear in the investigated ControlLab reports.

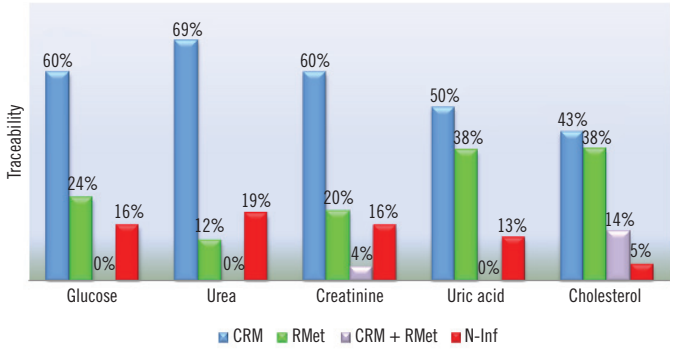

FIGURE – *Traceability of the analytical systems reported by the laboratories participating in the proficiency testing program of ControlLab, for determinations of glucose, urea, creatinine, uric acid, and cholesterol, during 2012 and 2013*

CRM: certified reference material; RMet: reference method; N-Info: no information on the use of CRM or RMet.

but not all RM products are registered in the databases COMAR and/or BIPM. For these cases, the survey was conducted directly on the producers' websites, for example, on ATCC.

When we compare RMets and the principles of methods for the measurands glucose, urea, creatinine, uric acid and cholesterol listed by JCTLM (Table 4) with the methods chosen by producers when metrological traceability was conferred by the use of RMet (Table 5), one can observe that the methods of the Clinical and Laboratory Standards Institute (CLSI) and of the American Association for Clinical Chemistry (AACC) do not appear in the JCTLM list, despite this is the choice by producers of the analytical systems Advia and Ebram. The survey conducted in the information of RMets supplied by diagnostic enterprises demonstrated that there is no standardization in the way to inform metrological traceability when one uses RMet. Some manufacturers inform the method principle,

such as, for instance, isotope dilution mass spectrometry (ID-MS); others, the institution that developed the method, for example, the Centers for Disease Control and Prevention (CDC). We could also observe that there are package inserts with outdated information, such as that of the analytical system Advia for the measurand glucose, which refers to CLSI mentioning the old acronym NCCLS.

In the metrological traceability informed through the use of CRM, RMet, CRM + RMet, and N-Info of analytical systems for determinations of glucose, urea, creatinine, uric acid, and cholesterol (Table 6 and Figure), we could observe that metrological traceability was presented at a higher percentage by the use of CRM (glucose 60%, urea 69%, creatinine 60%, uric acid 50%, and cholesterol 43%), and that an expressive number of analytical systems (glucose 16%, urea 19%, creatinine 16%, uric acid 13%, and cholesterol 5%) do not inform traceability.

Nowadays there is an international movement for the development of a measurement system reference, which encompasses CRM and RMet. Metrological traceability is considered one of the most important tools for the support of this process[24], what stimulates us to know and discuss this subject further.

CONCLUSION

Most of the 18 CRM producers are metrology institutes, and the number of RMs made available for clinical laboratories (a total of 204 measurands) is small contrasted with the number of conducted tests.

Concerning information on metrological traceability, most suppliers use CRM. There is an expressive number, ranging from 5% to 19%, of commercialized products in Brazil, which do not inform traceability, what reveals the little importance given to this piece of information by some diagnostic enterprises.

The laboratory community, including professionals that are part of them, is badly acquainted with the terms and concepts of metrological traceability and with its importance in laboratory results – although metrological traceability is a requirement in international guidelines applied to laboratories and in the national norm that rules product registration (RDC nº 206/2006).

This theme should be further discussed and studied by all the involved groups; and institutions related to the dissemination of knowledge in the area of clinical laboratories should make an effort to promote discussions about this issue.

We hope this study contributes to sensitize the laboratory community to the need for a more encompassing knowledge of the process of laboratory result production. We call special attention to the prior critical analysis of the diagnostic kits chosen by laboratories for routine use and the implications of this choice in their results.

RESUMO

Introdução: *Rastreabilidade metrológica é um tema da metrologia pouco conhecido e discutido nos laboratórios clínicos, apesar de ser a base para resultados comparáveis; associa-se a material de referência certificado (MRC) e a método de referência (MetR). Quando usada na cadeia de suprimentos pelos fabricantes de conjuntos diagnósticos, atua na garantia da exatidão dos resultados produzidos pelos laboratórios.* ***Objetivo:*** *Apresentar a disponibilidade das informações sobre rastreabilidade metrológica fornecidas pelos fabricantes de conjuntos diagnósticos.* ***Método:*** *O estudo foi feito com as informações obtidas nos conjuntos diagnóstico de glicose (GLI), ureia (URE), creatinina (CRE), ácido úrico (AU) e colesterol (COL) participantes de um programa de ensaio de proficiência ao longo de 2012 e 2013.* ***Resultados e conclusão:*** *Na pesquisa sobre produtores de materiais de referência (MRs) e de produtos disponibilizados, foram encontrados 18 produtores e 204 analitos para a área de laboratórios clínicos. No estudo sobre rastreabilidade metrológica, foi demonstrado o uso preferencial de MRC pelos fabricantes de conjuntos diagnósticos (GLI 60%; URE 69%; CRE 60%, AU 50% e COL 43%), bem como o dado importante de que há um número expressivo de conjuntos diagnósticos que não informa rastreabilidade (GLI 16%; URE 19%; CRE 16%, AU 13% e COL 5%), embora ela seja requisito em norma nacional que regulamenta o registro de produtos. Esperamos que este estudo contribua para sensibilizar a comunidade laboratorial da necessidade de conhecimento mais abrangente acerca deste assunto e que estimule as instituições relacionadas com a disseminação de conhecimento na área de laboratório clínico a promover discussões sobre o tema.*

Unitermos: *reagentes de laboratório; bioquímica.*

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